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TITLE: NRC/AMRMC Resident Research Associateship Program

PRINCIPAL INVESTIGATOR: Howard Gamble

CONTRACTING ORGANIZATION: NATIONAL ACADEMY OF SCIENCES
Washington, DC 20001

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| 14. ABSTRACT During this reporting period, the NRC promoted research opportunities at AMRMC institutes through a broad outreach plan. A total of 12 applications were received during the period and of these, 10 were reviewed by NRC panels. 8 awards were offered and all 8 were accepted. A total of 13 Associates ended their tenure during the reporting period and of these 9 submitted a final report. The productivity of these Associates is listed in the technical report. | | | | | |
| 15. SUBJECT TERMS- Associateship program, post-doc, awards | | | | | |
| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT UU | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON USAMRMC |
| a. REPORT U | b. ABSTRACT U | c. THIS PAGE U | | | 19b. TELEPHONE NUMBER (include area code) |

National Research Council
RESEARCH ASSOCIATESHIP PROGRAM
with
U.S. Army Medical Research & Materiel Command

Annual Contract Technical Report

Contract No. W81XWH-12-2-0010
Contract Period: 02/06/2012-02/05/2017

Contract No. W81XWH-12-2-0015
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Contract No. W81XWH-12-2-0033
Contract Period: 05/01/2012-04/30/2017

Contract No. W81XWH-12-2-0018
Contract Period: 03/15/2012-03/14/2017

Report Period: 05/01/2015-04/30/2016

During the reporting period, the NRC conducted the following activities in support of the subject contract:

Outreach and Promotion

The promotional schedule to advertise the National Research Council (NRC) Research Associateship Programs included the following: 1) attendance at meetings of major scientific and engineering professional societies; 2) advertising in programs and career centers for these and other professional society meetings; 3) direct mailing and emailing of announcements and program materials to presidents, graduate deans, and heads of appropriate science and engineering departments and minority-affairs offices of all academic degree-granting institutions in the United States; 4) posting announcements on internet job sites, electronic newsletters and professional society websites; 5) print advertising in high profile publications (e.g., Science magazine, the Chronicle of Higher Education); and, 6) maintaining a presence on social media sites such as Facebook.

The NRC attended a number of minority focused events in which we maintained exhibit booths, participated in workshops and advertised in meeting literature, newsletters and websites or submitted materials for distribution. In addition, ads were placed in a variety of minority publications (e.g., Affirmative Action, Black Collegian).

In advertising the Research Opportunities available to prospective applicants, the NRC maintained an up-to-date listing of all active Research Advisers, current Adviser contact information and details of each Research Opportunity.

Processing and Review of Applications

Applications to the Research Associateship Program were submitted via a web-based application system. Each of the four application cycles opened two months prior to the application deadline. NRC staff provided support to prospective applicants including providing application instructions, technical support and additional information as requested.

A summary of applications for the reporting period is shown in Table 1.

For each applicant, the NRC received and processed an application form, a research proposal, transcripts, a statement of previous and current research, and confidential reference reports. An application file check was made prior to the review and each applicant was notified if required documents were missing.

The NRC convened panels in five broad discipline areas for the competitive review of applications in the Research Associateship Programs. Results of the review were made available to Laboratory Program Representatives immediately following the conclusion of the each review.

A summary of the outcome of the review of applications for the reporting period is shown in Table 1.

Administration of Awards

The NRC made awards to applicants based on sponsor authorization. A summary of awards authorized and the acceptance or declination by the applicant during the current reporting period is shown in Table 1.

For Associates beginning or continuing tenure, the NRC provided the administrative functions described in the contract Statement of Work. These functions included stipend payments, management of a major medical benefits insurance program, and reimbursement for relocation and travel to professional meetings.

A summary of NRC Research Associates on tenure during the reporting period is shown in Table 2.

Outcomes Reporting

All NRC Associates who completed tenure were required to submit a final report that described the outcome of their Associateship award. Final reports received by the NRC during the current reporting period are attached to this technical report.

The activities of Associates submitting final reports during this reporting period, including publications, presentations and patents, as well as an assessment of their experience in the program, are summarized in Table 3. Specific research accomplishments of Associates completing tenure during the reporting period are summarized in Table 4.

Table 1. Applications and Awards

Table 2. Associates on Tenure

Table 3. Associates Activity

Table 4. Summary of Associate Research

Attachments: Associate Final Reports

U.S. Army Medical Research & Materiel Command

Table 1: Applications and Awards

| | May 2015 | Aug 2015 | Nov 2015 | Feb 2016 | Total |
|----------------------------|----------|----------|----------|----------|-------|
| TOTAL APPLICATIONS | 3 | 4 | 1 | 4 | 12 |
| Applications not reviewed | 1 | 1 | 0 | 0 | 2 |
| Applications reviewed | 2 | 3 | 1 | 4 | 10 |
| Not recommended | 0 | 0 | 0 | 0 | 0 |
| Recommended | 2 | 3 | 1 | 4 | 10 |
| Withdrawn | 0 | 0 | 0 | 0 | 0 |
| Lab decision pending | 0 | 0 | 0 | 2 | 2 |
| Awards offered | 2 | 3 | 1 | 2 | 8 |
| Applicant decision pending | 0 | 0 | 0 | 0 | 0 |
| Awards accepted | 2 | 3 | 1 | 2 | 8 |
| Awards declined | 0 | 0 | 0 | 0 | 0 |
| Not funded | 0 | 0 | 0 | 0 | 0 |

Table 2: Associates on Tenure

| Associate | Adviser | Tenure Dates | Country of Citizenship | Final Report |
|--|---------------------------|-----------------------|------------------------|--------------|
| U.S. Army Institute of Surgical Research | | | | |
| Benov, Avi | Darlington, Daniel Norman | 8/1/2014-7/31/2015 | Israel | Not Recv'd |
| Cheppudira, Bopaiah Pooviah | Christy, Robert John | 9/4/2012-9/3/2016 | India | |
| Choi, Jae hyek | Wang, Heuy-Ching H. | 11/15/2011-11/14/2015 | Korea, South | Not Recv'd |
| Greene, Whitney Ann | Wang, Heuy-Ching H. | 4/25/2012-4/24/2017 | United States | |
| Kaini, Ramesh Raj | Wang, Heuy-Ching H. | 1/3/2013-1/2/2016 | United States | Received |
| Karna, Sai Lakshmi Rajasekhar | Leung, Kai P | 4/1/2013-4/13/2017 | India | |
| Miller, Christine Lindsay | Leung, Kai P | 2/4/2013-2/3/2016 | United States | Received |
| Olekson, Melissa Ann | Leung, Kai P | 9/2/2014-9/1/2016 | United States | |
| Parida, Bijaya Kumar | Dubick, Michael A. | 3/19/2012-9/18/2016 | India | |
| Penn, Alexander Hayes | Torres Filho, Ivo P | 1/14/2015-1/13/2017 | United States | |
| Rose, Lloyd Frederick | Leung, Kai P | 11/1/2012-10/2/2015 | United States | Received |
| Salas, Margaux Marie | Clifford, John L | 10/10/2012-10/1/2015 | United States | Received |
| Sosanya, Natasha | Christy, Robert John | 4/20/2015-4/19/2017 | United States | |
| Van Laar, Tricia Annette | Leung, Kai P | 4/9/2012-7/29/2015 | United States | Received |
| U.S. Army Medical Research Institute of Chemical Defense | | | | |
| Beske, Phillip Howard | McNutt, Patrick Michael | 8/29/2013-8/28/2016 | United States | |
| Hubbard, Kyle | McNutt, Patrick Michael | 6/1/2012-5/31/2015 | United States | Received |
| U.S. Army Medical Research Institute of Infectious Diseases | | | | |
| Andrews, Elizabeth Susanne | Turell, Michael J | 5/13/2013-2/26/2016 | United States | Received |
| Bernhards, Robert Cory | Welkos, Susan Lee | 7/11/2013-4/29/2016 | United States | |
| Coate, Eric Allan | Bozue, Joel A | 12/30/2015-12/29/2016 | United States | |
| Cohen, Courtney Alicia | Glass, Pamela J | 7/28/2014-7/27/2016 | United States | |
| DeWald, Lisa Marie | Glass, Pamela J | 5/7/2012-5/6/2015 | United States | Not Recv'd |
| Duy, Janice | Minogue, Timothy Devins | 8/1/2013-7/31/2016 | United States | |
| Huse, Valerie | Minogue, Timothy Devins | 9/29/2014-9/28/2016 | United States | |
| Krishnamurthy, Malathy | Panchal, Rekha G. | 10/5/2015-10/4/2016 | India | |
| Mielech, Anna Maria | Ulrich, Robert Glenn | 2/2/2016-2/1/2017 | Poland | |
| O'Hearn, Aileen E | Schoepp, Randal J. | 4/1/2013-3/31/2016 | United States | Received |
| Ricks, Keersten Michelle | Schoepp, Randal J. | 12/7/2015-12/6/2016 | United States | |
| Shoemaker, Charles Jason | Schmaljohn, Connie | 2/3/2014-2/2/2017 | United States | |
| Smith, Jessica L | Ulrich, Robert Glenn | 6/24/2013-6/23/2016 | United States | |
| Stefan, Christopher Patrick | Minogue, Timothy Devins | 1/2/2014-1/1/2017 | United States | |
| Stojadinovic, Marija | Panchal, Rekha G. | 12/1/2014-11/30/2016 | Serbia | |
| Tursiella, Melissa Lynne | Schmaljohn, Connie | 4/1/2014-3/31/2017 | United States | |
| Zeng, Xiankun | Sun, Mei Guo | 5/4/2015-8/3/2016 | China | |
| Walter Reed Army Institute of Research, Silver Spring | | | | |
| Anderson, Margery Diane | Yourick, Debra Lynn | 3/11/2014-3/10/2017 | United States | |
| Barasa, Sheila Ogoma | Coldren, Rodney L. | 5/5/2015-5/4/2017 | Kenya | |
| DeDominicis, Kristen Elizabeth | Bryant, Ying Deng | 9/8/2015-9/7/2016 | United States | |
| Kobyliniski, Kevin Conrad | Davidson, Silas Andrew | 10/17/2011-10/16/2016 | United States | |
| Linton, Yvonne-Marie | Clark, Jeffrey William | 10/3/2011-10/2/2016 | United Kingdom | |
| McCracken, Michael Kevin | Jarman, Richard George | 3/9/2015-3/8/2017 | United States | |
| Pichard, Luis Eduardo | Balkin, Thomas J. | 7/24/2012-3/31/2016 | United States | Not Recv'd |
| Simonelli, Guido | Capaldi, Vincent F | 10/6/2014-10/5/2016 | Argentina | |
| Tenenbaum, Laura Subbiah | Yourick, Debra Lynn | 6/3/2013-6/2/2016 | United States | |
| Zarling, Stasya Nicole | Krzych, Urszula | 2/7/2011-8/6/2016 | United States | |

Table 3: Associates' Activities

- 13 Associates ended tenure during the report period
- 35 months was the average tenure length
- 48 months was the longest
- 11 months was the shortest
- 9 submitted final reports

In the final reports, Associates indicated the following scholarly activity while on tenure.

- 28 Articles published in refereed journals
- 0 Patent applications
- 2 International presentations
- 52 Domestic presentations
- 6 Awards

After ending their tenure, Associates indicated their future plans as follows:

- 0 Permanent position at the NRC host agency
- 3 Contract or temporary position at the NRC host agency
- 3 Research/administrative position with another U.S. government agency
- 0 Research/administrative position with foreign government agency
- 2 Research/teaching at US college/university
- 0 Research/teaching position at a foreign college or university
- 0 Research/administrative position in private industry in the U.S.
- 0 Research/administrative position in private industry outside of the U.S.
- 1 Research/administrative position with a non-profit
- 0 Self-employed/consulting
- 0 Postdoctoral Research
- 0 Other
- 0 No information provided

In their final reports, Associates were asked to evaluate certain aspects of their experiences on a scale of 1 (low) to 10 (high). The average rating for each item follows:

- 7.6 Short-term value (lab)-Development of knowledge, skills, and research productivity at lab
- 8.6 Long-term value (career)-How your Research Associateship affected your career to date
- 7.7 Laboratory Support-Equipment, funding, orientation, safety & health training, etc.
- 8.0 Adviser Mentoring-Quality of mentoring from the Research Adviser
- 7.7 LPR Support-Quality of administrative support from the LPR
- 8.6 NRC Support-Quality of administrative support from the NRC

Table 4: Summary of Associate Research

| Associate | | Tenure Dates |
|---------------------------|---|----------------------------|
| Andrews, Elizabeth | | 5/13/2013-2/26/2016 |
| 1 | Examined the effect of Wolbachia infection in Culex tarsalis on infection, dissemination, and transmission of Rift Valley fever virus. Viral titers of blood fed mosquitoes were determined and correlated to Wolbachia density using quantitative PCR. | |
| 2 | Screened plasma containing different ApoL1 isoforms and recombinant ApoL1 protein isoforms against a range of pathogens that are endemic to West Africa to determine which ones are restricted by ApoL1. | |
| 3 | Conducted an ecological study of the mosquitoes of the Patuxent Research Refuge in Laurel, MD summer 2015. Identified species, analyzed bloodmeals, and tested for viruses. | |
| 4 | Examined the effect of filarial nematodes in robins and grackles on the dissemination and transmission rates of West Nile virus by Culex pipiens. | |
| Bernhards, Robert | | 7/11/2013-4/29/2016 |
| 1 | New lipopolysaccharide (LPS) subtypes were discovered in Burkholderia pseudomallei. | |
| 2 | An LPS change was observed in Burkholderia mallei during the course of mouse infection. | |
| 3 | Discovered two stable variants of Burkholderia pseudomallei strain MSHR5848 that expressed broadly divergent in vitro phenotypes. | |
| Hubbard, Kyle | | 6/1/2012-5/31/2015 |
| 1 | Developed a protocol to generate synaptic activity in neurons derived from human induced pluripotent stem cells (ongoing). | |
| 2 | Used transcriptomics and differential gene expression analysis to define developmental milestones during mouse embryonic stem cell differentiation and neuronal maturation. | |
| 3 | Evaluated time- and dose-dependent progression of excitotoxic injury using mouse embryonic stem cell-derived neurons as a platform. | |
| 4 | Helped develop a medium-throughput assay for the functional evaluation of neuromodulatory biothreat agents. | |
| 5 | Utilized proteomics, transcriptomics and functional assays to investigate the cellular and molecular mechanisms underlying excitotoxicity in a physiologically relevant in vitro model. | |
| Kaini, Ramesh | | 1/3/2013-1/2/2016 |
| 1 | Optimize maintenance and propagation of human iPSC cells in a defined and xenofree condition. | |
| 2 | Xenofree differentiation of hiPS cells into neuro-retina | |
| 3 | Generation of photoreceptors like cells from human iPS cells | |
| 4 | Studied the dynamics of extracellular matrix remodeling during retinogenesis | |
| 5 | Formulate a research plan on using stem-cell released molecule as a therapy in blast-injured retina | |
| Miller, Christine | | 2/4/2013-2/3/2016 |
| 1 | Optimized protocol to isolate, identify, and categorize small RNAs (sRNAs) for the discovery of small regulatory RNAs. | |
| 2 | Utilized a custom RNA-sequencing method to unbiasedly capture the global transcriptome response of pathogens typically present in war wounds and which hinder healing. | |
| 3 | Used an in vitro model to investigate the interactions of P. aeruginosa and S. aureus in biofilm and planktonic cultures | |
| 4 | Discovered sRNAs that play a key role in modulating interspecies interactions in the biofilm, and required for the adaptive switch between acute and chronic infection phenotypes. | |
| 5 | Generated numerous protocols to genetically engineer P. aeruginosa and analyze phenotypes of various mutants. | |
| O'Hearn, Aileen | | 4/1/2013-3/31/2016 |
| 1 | Development of a pan-Flavivirus and pan-Alphavirus IgG test to be incorporated in a panel of African viral diagnostics | |
| 2 | Development of a multi-target serosurveillance test for identifying viral pathogens in West Africa | |
| 3 | Serosurvey of a Sierra Leonean population for the presence of viral pathogens, and identification of public health threats | |
| 4 | Development and testing of a Lassa virus diagnostic testing panel for identifying human Lassa Fever cases | |
| 5 | On-site support during the West African Ebola outbreak | |
| Rose, Lloyd | | 11/1/2012-10/2/2015 |
| 1 | Establishment of a porcine model of skin loss correlating thickness of autologous skin graft with amount of contraction after 120 days. | |
| 2 | Autologous skin grafts grafted onto fat (as opposed to grafting onto deeper tissues) resist contractile forces induced by myofibroblasts | |

| | |
|-----------------------------|---|
| 3 | Burn wounds have increased inflammatory markers and have increased levels of wound contraction compared to skin loss by non-burn mechanisms. |
| 4 | Application of ultra-high dose gentamicin to the wound bed induces an anti-angiogenic gene expression profile in vivo as well as inducing genetic and phenotypic alterations in endothelial cells and macrophages in tissue culture. |
| Salas, Margaux | |
| 10/10/2012-10/1/2015 | |
| 1 | Tetrodotoxin Attenuates Thermal Hyperalgesia in a Rat Full Thickness Thermal Injury Pain Model |
| 2 | Curcumin is an Effective Analgesic for Burn Pain: Evidence from Animal and Human Tissue Based Experiments |
| 3 | Resiniferatoxin: A Potential Burn Analgesic for Point of Injury/Battlefield |
| Van Laar, Tricia | |
| 4/9/2012-7/29/2015 | |
| 1 | Contributed to gene sequencing of multi-drug resistant <i>Klebsiella pneumoniae</i> . |
| 2 | Performed transcriptome analysis of multi-drug resistant <i>K. pneumoniae</i> and identified numerous genes for downstream analysis in combating multi-drug resistant <i>K. pneumoniae</i> . Also described molecular mechanisms for significant morphological changes. |
| 3 | Performed transcriptome analysis of mixed species biofilm and planktonic cultures of <i>Staphylococcus aureus</i> and <i>Pseudomonas aeruginosa</i> and identified numerous ORFs necessary for competition between these two species. |
| 4 | Performed transcriptome analysis of persister cells of <i>P. aeruginosa</i> to identify ORFs necessary for persister cell formation, and therefore lack of healing in <i>P. aeruginosa</i> infected wounds. |

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|--|---|
| 1) Associate Last or Family Name | First Name | M.I. |
| Andrews | Elizabeth | S |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | |
| Residence or Institution Street City, State Zip | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: | |
| 3) Today's Date | | |
| February 15, 2016 | Dates of Tenure from May 13, 2013 to February 26, 2016 | |
| 4) Host Agency US Army (e.g., AFRL) | Laboratory or Center USAMRIID (e.g., Wright Patterson AFB) | Division / Directorate / Department Virology (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) | | |
| Michael Turell | | |

6) *TITLE OF RESEARCH PROPOSAL*

Effect of environmental factors on the ability of North American mosquitoes to transmit Rift Valley fever virus

7) *SUMMARY OF RESEARCH DURING TENURE* Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Examined the effect of Wolbachia infection in *Culex tarsalis* on infection, dissemination, and transmission of Rift Valley fever virus. Viral titers of blood fed mosquitoes were determined and correlated to Wolbachia density using quantitative PCR
- 2) Screened plasma containing different ApoL1 isoforms and recombinant ApoL1 protein isoforms against a range of pathogens that are endemic to West Africa to determine which ones are restricted by ApoL1.
- 3) Conducted an ecological study of the mosquitoes of the Patuxent Research Refuge in Laurel, MD summer 2015. Identified species, analyzed bloodmeals, and tested for viruses.
- 4) Examined the effect of filarial nematodes in robins and grackles on the dissemination and transmission rates of West Nile virus by *Culex pipiens*.

5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) *RESEARCH IN PROGRESS* Describe in no more than 100 words.

I am currently finishing up the ecological study of the mosquito fauna of the Patuxent Research Refuge in Laurel, MD. Blood meal analysis and viral isolation is being performed in the mosquitoes collected. This will be continued for me by the members of my laboratory.

9) *PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

E. S. Andrews, G. B. Schoeler, A. S. Gozalo, F. Carbajal, V. Lopez-Sifuentes, and M. J. Turell. (2014). Species Diversity, Seasonal, and Spatial Distribution of Mosquitoes (Diptera: Culicidae) Captured in Aotus Monkey-Baited Traps in a Forested Site Near Iquitos, Peru. Journal of Medical Entomology 51(6): 1127-1135.

E. S. Andrews and M. J. Turell (in press). Effect of holding conditions on the detection of chikungunya and Venezuelan equine encephalitis viruses in mosquito pools. Journal of the American Mosquito Control Association.

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

T. Kutateladze, E. Zangaladze, N. Dolidze, T. Mamatsashvili, L. Tskhvaradze, E. S. Andrews, and A. D. Haddow (submitted) First record of *Aedes albopictus* (Diptera: Culicidae) in Georgia and updated checklist of reported species. *Journal of Vector Ecology*

E. S. Andrews, B. L. Dodson, M. J. Turell, and J. L. Rasgon (in prep) Artificial *Wolbachia* infections in *Culex tarsalis* do not affect transmission of Rift Valley fever virus.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

None

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

None

Domestic

American Mosquito Control Association Annual Meeting. February 7-11, 2016, Savannah, GA: E. S. Andrews. Talk. Highlights in Vector Biology 2015.

Reviewed in this presentation is a selection of the published literature on the biology of arthropod vectors of human disease from the 2015 calendar year. Manuscripts were chosen based on their potential impact to the field of vector biology. Several major groups of disease vectors, such as mosquitoes, ticks, sand flies, and lice will be discussed. Topics will be broadly reviewed and include species descriptions, phylogeny, genetics, behavior, physiology, ecology, and pathogen transmission. Emphasis will be placed on articles effecting control practices and the epidemiology of associated pathogens such as parasites, bacteria and viruses. The objective of this review is to synthesize the new literature across a breadth of vector biology topics into a manageable format for the listener.

NICBR Spring Research Festival. May 5, 2015, Fort Detrick, MD. E. S. Andrews, S. Limou, M. J. Turell, and C. Winkler. Talk. ApoL1 restrictive effects on West African pathogens.

American Society of Tropical Medicine and Hygiene Annual Meeting, Nov. 2-5, 2014, New Orleans, LA: E.S. Andrews and M.J. Turell. Poster. Effect of holding conditions on the detection of chikungunya and Venezuelan equine encephalitis virus in mosquito pools.

Abstract: Emerging and re-emerging arboviruses continue to be a threat to global public health. With the recent introduction of chikungunya virus (CHIKV) into the Caribbean and its potential spread across the Americas, there will be a need to increase surveillance of mosquito populations for viruses. Due to the tropical climate of many of the affected areas, it will be difficult to maintain a cold chain as the samples travel from collection sites to laboratories for testing. We determined how suboptimal holding temperatures affected the ability to detect viruses in pools of mosquitoes. Adult female *Aedes albopictus* and *Aedes taeniorynchus* were inoculated with CHIKV or Venezuelan equine encephalitis virus (VEEV) suspensions, respectively, and placed at 26°C for 7 days. One infected mosquito was then added to a vial of 24 negative mosquitoes and then held at -70°C, -20°C, 4°C, 22°C, or 35°C for selected time intervals. Mosquito pools were triturated in cell culture media and processed for detection of CHIKV and VEEV. Samples were analyzed for both infectious virus by plaque assay and for viral RNA with real-time RT-PCR. At high temperatures the amount of infectious virus decreased rapidly, but virus in samples held at 4°C or lower remained relatively stable. In contrast, viral RNA was detectable from pools held at all temperatures and holding times by real-time RT-PCR, although Ct values increased as temperatures and holding times increased. These findings suggest that if viral RNA detection is the goal of surveillance efforts, then mosquito pools do not need to be kept at 4°C. This enhances the feasibility of field-based arbovirus surveillance programs where maintaining a cold chain may not be a possibility.

Northeastern Eastern Equine Encephalitis Conference Annual Meeting. May 9, 2014, Concord, NH: Andrews, E.S. Invited talk. Future control strategies involving the microbial communities of mosquitoes.

Abstract: Classic control methods for mosquitoes involve habitat modification to prevent oviposition and larval development, chemical control with pesticides to reduce the densities of both immatures and adults and biological control with parasites, predators and pathogens. While sometimes effective, there are inherent issues associated with these control methods. Source reduction, chemical and biological control all require direct application to the targeted mosquito population. Many adult and larval populations can be difficult to access due to cryptic habitats and breeding sites. In some cases insecticide application is not cost-effective due to the vastness of targeted areas or beneficial for the environment, as multiple applications of insecticides can have detrimental effects on non-target insect populations. In addition, insecticide resistance has developed in major disease vectors, necessitating the development of new and sustainable mosquito control strategies. The utilization of bacteria within mosquitoes may be a potential avenue for the development of novel control approaches to offset these setbacks. Initial studies observed that alteration of the bacterial community affected *Cx. quinquefasciatus* susceptibility to Japanese encephalitis virus and reduced *Plasmodium* oocyst density in *An. albimanus*. In *Ae. aegypti*, the bacterial

community can affect the dynamics of dengue virus, in which the level of virus titer is dependent on the presence of specific bacterial taxa. *Wolbachia*, a maternally inherited bacterial endosymbiont observed in mosquitoes has received attention as a potential tool for mosquito-borne disease control. For example, bidirectional incompatibility can be induced in mosquito populations in which there is a *Wolbachia* infection already present. In these scenarios, releases of incompatible males are used to suppress the existing mosquito population via sterility resulting from incompatible crosses. Another series of *Wolbachia*-based control efforts focuses on the ability of the bacterium to spread itself into uninfected mosquito populations using the reproductive advantage afforded to it by unidirectional CI. In these applications, the focus is modification, rather than elimination of the vector population. Refractory phenotypes or transgenes that prevent disease transmission could be driven into a mosquito population using *Wolbachia*-mediated population replacement.

American Mosquito Control Association annual meeting, Feb. 2-6, 2014, Seattle, WA: E. S. Andrews and S. L. Dobson. Investigating dynamics of the bacterium *Asaia*, a potential paratransgenic disease control method, within *Aedes albopictus*. *Asaia*, an acetic acid bacterium, has gained interest as a potential novel method of paratransgenic mosquito-borne disease control due to its direct association with mosquitoes of medical importance. To determine if the bacterium is an associate of *Ae. albopictus*, *Asaia* infection dynamics were investigated. The microbial community within *Ae. albopictus* was compared between field-collected and laboratory-reared females and their eggs using DGGE. *Asaia* was detected within both types of females, but not within egg pools. Culturing *Asaia* from field-collected mosquitoes yielded two genetically different isolates, both of which are >99% identical with those isolated in previous studies. Field experiments involved collection of wild populations of *Ae. albopictus* and flowering plants as possible sources of *Asaia*. These experiments determined that there was seasonal and yearly variation in our ability to detect *Asaia* in the environment. Laboratory experiments observed that the bacterium was continuously associated with *Ae. albopictus* for the duration of its lifespan, although rates of infection within the population were not 100%. *Asaia* was present in midguts and testes, but rarely ovaries, possibly indicating a lack of vertical transmission routes. The results indicate that, although *Asaia* may associate with *Ae. albopictus*, it may not be a facultative symbiont, as observed in other mosquito species, and may be opportunistically acquired from the mosquito's environment.

American Society of Tropical Medicine and Hygiene annual meeting, Nov. 13-16, 2013, Washington, DC: M. J. Turell, S. C. Britch, R. L. Aldridge, E. S. Andrews, B. D. Byrd, B. A. Harrison and K. J. Linthicum.

An update on the potential for North American mosquitoes to transmit Rift Valley fever virus

The introduction of West Nile virus into the U.S. in 1999 and its subsequent spread across North America illustrates the potential for an exotic arbovirus to be introduced and become established in North America and to cause significant disease and economic disruption. Infection with Rift Valley fever virus (RVFV) can cause severe disease in cattle, goat, and sheep, with nearly 100% mortality in new-borne animals and nearly 100% abortion in pregnant ones. This mosquito-borne virus has been responsible for numerous outbreaks in domestic ruminants and humans in sub-Saharan Africa over the past 80 years and there is concern of what might happen if it were introduced into North America. Therefore, in order to identify potential mosquito vectors that should be prioritized for control, should it be introduced, we evaluated a number of North American mosquito species for their susceptibility to infection and their ability to transmit RVFV by bite.

When exposed to hamsters infected with RVFV, at least some individuals in each of the 28 mosquito species tested became infected. Several species, including *Cx. nigripalpus*, *Cx. quinquefasciatus*, *Cx. salinarius*, and *Ae. vexans* (from the northwest), were barely susceptible to infection. Despite some species having high infection and dissemination rates, species with significant salivary gland barriers were essentially incompetent vectors in the laboratory. Species with a significant salivary gland barrier included *Ae. aegypti*, *Ae. albopictus*, *Ae. dorsalis*, *Ae. infirmatus*, *An. crucians*, *An. quadrimaculatus*, *Cx. quinquefasciatus*, *Ps. ciliata* and *Ps. columbiae*. Based on susceptibility to infection, viral dissemination, lack of salivary gland barrier, abundance, and feeding preference, the species that have the greatest potential to transmit RVFV in North America are *Ae. canadensis*, *Ae. japonicus*, *Ae. sollicitans*, *Ae. taeniorhynchus*, *Cq. perturbans*, *Cx. tarsalis*, and *Ps. ferox* and should be prioritized for control. Additional studies need to be conducted with other relevant mosquito species, different geographic populations and to determine how environmental factors, such as temperature and the presence of other pathogens, affect transmission.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

National Interagency Confederation for Biological Research Collaborative Project Award. 2014. ApoL1 restrictive effects on West African pathogens. Ft. Detrick, MD, \$20,000

14) *POST-TENURE POSITION / JOB TITLE*

Associate Public Health Biologist

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

California Department of Public Health. Vector-borne Disease Division

16) *POST-TENURE POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | |
| <input checked="" type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- 1)
- 2)
- 3)
- 4)
- 5)

18) *APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

6 Development of knowledge, skills, and research productivity

Comments

I gained excellent knowledge of how to conduct work with viruses in upper level containment, BSL-3 and BSL-4. The skills I gained I could not have received anywhere else. However, my research was not even close to how productive I would have liked it due to renovations, delays when receiving reagents, and personnel issues.

LONG TERM VALUE

5 How the NRC Research Associateship award affected your career to date

Comments

The associateship has given me experience working internationally and with upper level containment viruses. It looks great on my resume. I wish I could have actually conducted publishable research.

LAB SUPPORT

2 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

The equipment was archaic and from 30 years ago. When I attempted to purchase new equipment with my funds, I was argued with the ultimately prevented from doing so by my advisor. I scrambled to beg other labs to use equipment and reagents. The ordering system took far too long to receive equipment. It took me close to a year to receive artificial bloodfeeders. 3 months was the minimum for reagents I would have received within a week at another institution.

ADVISER/MENTOR SUPPORT

3 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)

Comments

While my adviser was a very nice person, he was a terrible mentor. He constantly fought with me when I wanted to buy equipment and do cutting edge techniques. I had to follow his methods exactly. And he retired prior to the end of my tenure as a post doc.

LPR SUPPORT

9 Quality of administrative support from the Laboratory Program Representative (LPR)

Comments

The administrative support was great. No complaints.

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

9 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

No complaints. Everything was really efficient.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator
No handwritten signature required;

*but you may upload a scanned
signature file below:*

Leah Probst: lprobst@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. October 2015

Proj/Act ID#

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|---|---|
| 1) Associate Last or Family Name | First Name | M.I. |
| Bernhards | Robert | C |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | |
| Residence or Institution Street City, State Zip | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: | |
| 3) Today's Date | | |
| April 13, 2016 | Dates of Tenure from July 10, 2013 to April 20, 2016 | |
| 4) Host Agency AMRMC (e.g., AFRL) | Laboratory or Center USAMRIID (e.g., Wright Patterson AFB) | Division / Directorate / Department Bacteriology (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) | | |
| Susan Welkos | | |

6) **TITLE OF RESEARCH PROPOSAL**

LPS diversity among Burkholderia mallei and Burkholderia pseudomallei and the association with acute and chronic infection

7) **SUMMARY OF RESEARCH DURING TENURE** Itemize significant findings in concise form, utilizing key concepts/words.

- 1) New lipopolysaccharide (LPS) subtypes were discovered in Burkholderia pseudomallei.
- 2) An LPS change was observed in Burkholderia mallei during the course of mouse infection.
- 3) Discovered two stable variants of Burkholderia pseudomallei strain MSHR5848 that expressed broadly divergent in vitro phenotypes.

4)

5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) **RESEARCH IN PROGRESS** Describe in no more than 100 words.

We are currently developing a peptide mimotope vaccine that is cross-protective against Burkholderia pseudomallei and Burkholderia mallei using peptides that mimic Burkholderia lipopolysaccharide (LPS) and capsular polysaccharide (CPS). These peptides are being conjugated to carrier protein CRM197, and the conjugates will be tested for protection from Burkholderia infection in mice.

9) **PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH**

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

Welkos, S.L., Klimko, C.P., Kern, S., Bearss, J., Bozue, J.A., Bernhards, R.C., Trevino, S.R., Dankmeyer, J.L., Waag, D.M., Worsham, P.L., Amemiya, K., and Cote, C.K. (2015) Characterization of Burkholderia pseudomallei strains using a murine intraperitoneal infection model and in vitro macrophage assays, PLOS ONE. 10.

Alam, S., Amemiya, K., Bernhards, R.C., Ulrich, R.G., Waag, D.M. and Saikh, K.U. (2015) Characterization of cellular immune response and innate immune signaling in human and nonhuman primate primary mononuclear cells exposed to Burkholderia mallei, Microbial Pathogenesis. 78, 20-28.

Omotade, T.O., Bernhards, R.C., Matthews, M., Klimko, C.P., Hill, A., Hunter, M., Bozue, J.A., Welkos, S.L., Cote, C.K. (2014) The impact of Bacillus anthracis and Bacillus thuringiensis spore germination state on potential secondary decontamination strategies, Journal of Applied Microbiology. 117, 1614-1633.

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

Bernhards, R.C., Weaver, C., Guo, P., Zhang, J., Li, B., Worsham, P.L., Lo, S-H., and Welkos, S.L. Developing peptide mimotope vaccines for melioidosis and glanders.

Bernhards, R.C., Shea, A.A., Cote, C.K., Rozak, D.A., Wolcott, M.J., Fetterer, D., Kern, S., Worsham, P.L., Ladner, J.T., Koroleva, G.I., Lovett, S.P., Toothman, R., Bozue, J., and Welkos, S.L. Two stable variants of *Burkholderia pseudomallei* strain MSHR5848 express broadly divergent in vitro phenotypes associated with their virulence differences.

Bernhards, R.C., Cote, C.K., Amemiya, K., Waag, D.M., Klimko, C.P., Worsham, P.L., Welkos, S.L. Characterization of in vitro phenotypes of *Burkholderia pseudomallei* and *Burkholderia mallei* strains potentially associated with persistent infection in mice.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Bernhards, R.C., Hill, A. J, Trevino, S. R., Waag, D. M., Cote, C. K., Welkos, S. L. March 26–27, 2015. LPS characterization of *Burkholderia pseudomallei* strains. Poster presentation at the European Melioidosis Congress, Cambridge, United Kingdom.

Domestic

Bernhards, R.C., Weaver, C.H., Guo, P., Zhang, J., Li, B., Lo, S-H., and Welkos, S.L. May 4, 2016 (upcoming). Developing Peptide Mimotope Vaccines for Melioidosis and Glanders. Spring Research Festival Research Collaboration Forum, Fort Detrick, MD.

Bernhards, R.C., Guo, P., Zhang, J., Li, B., Weaver, C.H., Lo, S-H., and Welkos, S.L. February 8–10, 2016. Developing Peptide Mimotope Vaccines for *Burkholderia*. Poster presentation at the American Society for Microbiology (ASM) Biodefense & Emerging Diseases Research Meeting, Arlington, VA.

Bernhards, R.C., Hill, A. J, Trevino, S.R., Waag, D.M., Cote, C.K., Welkos, S. L. May 4, 2015. Characterization of *Burkholderia* LPS and elucidating its role in acute and chronic infections. Selected to be Bacterial Pathogenesis and Characterization session chair and awarded Outstanding Oral Presentation at the National Interagency Confederation for Biological Research (NICBR) Spring Research Festival, Fort Detrick, MD.

Bernhards, R.C., Hill, A.J., Trevino, S. R., Waag, D.M., Cote, C.K., Welkos, S.L. February 11, 2015. LPS characterization of *Burkholderia mallei* and *Burkholderia pseudomallei* strains. Poster presentation at the ASM Biodefense & Emerging Diseases Research Meeting, Washington, D.C.

Bernhards, R.C., Hill, A.J., Trevino, S.R., Waag, D.M., Cote, C.K., Welkos, S.L. May 20, 2014. LPS diversity among strains of *Burkholderia mallei* and *Burkholderia pseudomallei*. Poster presentation at the General Meeting of the ASM, Boston, MA.

Bernhards, R.C., Hill, A.J, Trevino, S.R., Waag, D.M., Cote, C.K., Welkos, S.L. May 5, 2014. LPS Diversity among Strains of *Burkholderia mallei* and *Burkholderia pseudomallei*. Selected oral presentation at the 2014 National Interagency Confederation for Biological Research (NICBR) Spring Research Festival, Fort Detrick, MD.

Bernhards, R.C., Hill, A.J, Trevino, S.R., Waag, D.M., Cote, C.K., Welkos, S.L. January 28, 2014. LPS diversity among strains of *Burkholderia mallei* and *Burkholderia pseudomallei*. Poster presentation at the ASM Biodefense & Emerging Diseases Research Meeting, Washington, D.C.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

Bernhards, R.C., Weaver, C.H., Guo, P., Zhang, J., Li, B., Lo, S-H., and Welkos, S.L. March 8, 2016. Developing Peptide Mimotope Vaccines for Melioidosis and Glanders. Edgewood Chemical Biological Center (ECBC) Seminar, Aberdeen Proving Ground, MD.

Bernhards, R.C., Trevino, S. R., Waag, D. M., Hill, A.J., Weaver, C.H., Guo, P., Zhang, J., Li, B., Nasar, F., Lo, S-H., and Welkos, S.L. October 23, 2015. USAMRIID Biodefense Research: Burkholderia. Guest Lecture for Microbial Forensics & Biosecurity class at Virginia Tech, Blacksburg, VA.

Bernhards, R.C., Amemiya, K., Hill, A.J., Trevino, S.R., Waag, D.M., Cote, C.K., Welkos, S.L. June 10, 2015. Characterization of Burkholderia LPS and elucidating its role in acute and chronic infections. USAMRIID NRC Seminar, Fort Detrick, MD.

Bernhards, R.C., Hill, A.J., Trevino, S.R., Waag, D.M., Omotade, T.O., Klimko, C.P., Matthews, M.E., Hunter, M.S., Cote, C.K., Welkos, S.L. December 1, 2014. USAMRIID Biodefense Research: Burkholderia and Bacillus anthracis. Guest Lecture for Microbial Forensics & Biosecurity class at Virginia Tech, Blacksburg, VA.

Bernhards, R.C., Hill, A.J., Trevino, S.R., Waag, D.M., Cote, C.K., Welkos, S.L. June 4, 2014. LPS Phenotypic Differences among Strains of Burkholderia mallei and Burkholderia pseudomallei. USAMRIID NRC Seminar, Fort Detrick, MD.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

2015 National Interagency Confederation for Biological Research (NICBR) Collaborative Project Grant

Co-PI on Defense Threat Reduction Agency (DTRA) Grant: Development of vaccines protective against Burkholderia pseudomallei and Burkholderia mallei

Outstanding Presentation Award at the NICBR Scientific Symposium, May 2015

14) *POST-TENURE POSITION / JOB TITLE*

Research Microbiologist (PI, civilian-term)

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

**US Army Edgewood Chemical Biological Center
AMSRD-ECB-PI-BP-CP/Kennedy E3330
5183 Blackhawk RD
APG, MD 21010-5424**

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | <input type="checkbox"/> Research/administration position with a non profit |
| <input checked="" type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* **Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.**

- 1)
- 2)
- 3)
- 4)
- 5)

18) *APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

9 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

10 How the NRC Research Associateship award affected your career to date
Comments
Wouldn't have been able to obtain new PI position without this associateship.

LAB SUPPORT

9 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

Very good funding.

ADVISER/MENTOR SUPPORT

8 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)

Comments

LPR SUPPORT

6 Quality of administrative support from the Laboratory Program Representative (LPR)

Comments

Both LPRs during my tenure were not very proactive in organizing meetings/seminars and did nothing to encourage fellow NRC associates to network or get to know one another.

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

10 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

Easy to communicate with and very efficient.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator

No handwritten signature required;

but you may upload a scanned

signature file below:

Leah Probst: lprobst@nas.edu

Linda Sligh: lsligh@nas.edu

Melanie Suydam: msuydam@nas.edu

Peggy Wilson: pwilson@nas.edu

Id#

Rev. October 2015

Proj/Act ID#

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine
National Research Council

Research Associateship Programs

FINAL REPORT

| | | | |
|--|------------------------------|---|------|
| 1) Associate Last or Family Name | | First Name | M.I. |
| Hubbard | | Kyle | S |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | FORWARDING Phone(s) and E-Mail (if known) | |
| Residence or Institution Street | | Home Phone: N/A | |
| City, State Zip | | Alt. Phone: | |
| | | Preferred E-mail: | |
| 3) Today's Date | | Dates of Tenure | |
| May 28, 2015 | | from June 1, 2012 to May 31, 2015 | |
| 4) Host Agency | Laboratory or Center | Division / Directorate / Department | |
| AMRMC | USAMRICD | Research Division/Cellular Molecular Bio | |
| (e.g., AFRL) | (e.g., Wright Patterson AFB) | (e.g., High-Speed Propulsion) | |
| 5) Name of Laboratory NRC Adviser (and USMA Mentor, if applicable) | | | |
| Patrick McNutt | | | |

6) TITLE OF RESEARCH PROPOSAL

Transcriptome and functional analysis of excitotoxic mechanisms using embryonic stem cell-derived glutamatergic neurons

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Developed a protocol to generate synaptic activity in neurons derived from human induced pluripotent stem cells (ongoing).
- 2) Used transcriptomics and differential gene expression analysis to define developmental milestones during mouse embryonic stem cell differentiation and neuronal maturation.
- 3) Evaluated time- and dose-dependent progression of excitotoxic injury using mouse embryonic stem cell-derived neurons as a platform.
- 4) Helped develop a medium-throughput assay for the functional evaluation of neuromodulatory biothreat agents.
- 5) Utilized proteomics, transcriptomics and functional assays to investigate the cellular and molecular mechanisms underlying excitotoxicity in a physiologically relevant in vitro model.

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

N/A

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Development of synaptically active, networked neurons derived from induced human pluripotent stem cells for toxin detection and therapeutic screening

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

McNutt, P., Gut, I., Hubbard, K. and Beske, P. A novel method to prioritize RNAseq data for post-hoc analysis based on absolute changes in transcript abundance. *Stat Appl Genet Mol Biol*, (in press).

Hubbard, K.S., Beske, P.H., Lyman, M.E. and McNutt, P.M. Functional evaluation of biological neurotoxins using synaptically active, networked cultures of stem cell-derived central nervous system neurons. *J. Vis. Exp.*, 2015, (96), e52361, doi:10.3791/52361.

Gut, I.M., Beske, P.H., Hubbard, K.S., Lyman, M.E., Hamilton, T.A. and McNutt, P. Novel application of stem cell-derived neurons to evaluate time- and dose-dependent progression of excitotoxic injury. *PLoS One*, 2013, 8(5):e64423.

Andres, D., Keyser, B., Petralli, J., Benton, B., Hubbard, K., McNutt, P. and Ray, R. Morphological and Functional Differentiation in BE(2)-M17 Human Neuroblastoma Cells by Treatment with Trans-Retinoic Acid. *BMC Neuroscience*, 2013, 14(1):49.

Hubbard K.S., Gut I.M., Lyman M.E. and McNutt, P.M.. (2013) Longitudinal RNA sequencing of the deep transcriptome during neurogenesis of cortical glutamatergic neurons from murine ESCs [v1; ref status: approved 1, <http://f1000r.es/w2>] F1000Research 2013, 2:35 (doi: 10.3410/f1000research.2-35.v1)

Hubbard, K., Gut, I.M., Lyman, M., Tuznik, K. and McNutt, P. High yield derivation of enriched glutamatergic neurons from suspension-cultured mouse ES cells for neurotoxicology research. BMC Neuroscience, 2012, 13:127. Highly Accessed.

Hubbard, K., Gut, I.M., Scheeler, S.M., Lyman, M. and McNutt, P.M.. SYTO 13 is neurotoxic in longitudinal imaging assays, and prevents nuclear condensation in neurons following staurosporine treatment. BMC Research Notes, 2012, 5:437.

b) Books, book chapters, other publications

N/A

c) Manuscripts in preparation, manuscripts submitted

Hubbard, K., Beske, P., Glotfelty, E., Lyman, M. and McNutt, P. Functional evaluation and longitudinal expression profiling of neuronal differentiation from murine embryonic stem cells.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

N/A

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

N/A

Domestic

Hubbard, K. A functionally relevant human pluripotent stem cell-derived neuron-based platform to measure the potency of botulinum neurotoxin. Gordon Research Seminar for Chemical and Biological Terrorism Defense. Ventura, CA, March 2015.

Hubbard, K., Hoffman, K., Beske, P., Glotfelty, E., Hamilton, T. and McNutt, P. Functional synaptic activity and network emergence in human stem cell-derived neurons: towards a relevant in vitro model of human CNS neurons. Society for Neuroscience Annual Meeting. Washington, DC, November 2014.

Hubbard, K. Stem cell-derived neurons as a physiologically relevant platform to investigate cellular mechanisms underlying excitotoxicity. CounterACT Network Research Symposium. Denver, CO, June 2014.

Hubbard, K., Gut, I., Glotfelty, E., Beske, P., Hamilton, T. and McNutt, P. Functional synaptic activity and network emergence in human stem cell-derived neurons: towards a relevant in vitro model of human CNS neurons? US Army Medical Defense Bioscience Review. Hunt Valley, MD, May 2014.

Hubbard, K., Beske, P. and McNutt, P. Correlation Of Transcriptomic And Functional Changes During Neuronal Maturation In ESC-Derived Neurons. Maryland Stem Cell Research Symposium. Baltimore, MD, December 2013.

Hubbard, K., Gut, I., Beske, P., Lyman, M.E. and McNutt, P. Cellular and molecular correlates of glutamate-induced excitogenic injury in mouse stem cell-derived neurons. Society for Neuroscience Annual Meeting. San Diego, CA, November 2013.

Hubbard, K., Gut, I., Beske, P. and McNutt, P. Mechanistic characterization of glutamatergic excitotoxicity in embryonic stem cell-derived neurons. Countermeasures Against Chemical Threats Network Research Symposium. Bethesda, MD, June 2013.

Hubbard K., Gut, I., Glotfelty, E., Beske, P., Lyman, M. and McNutt, P. Embryonic stem cell-derived neurons offer a robust model for the study of neuronal induction and cortical neurogenesis. Gordon Research Conference. Ventura, CA, March 2013.

Hubbard, K., Gut, I., Lyman, M. and McNutt, P. Longitudinal expression profiling of neuronal differentiation from neural progenitor cells using next generation sequencing. Maryland Stem Cell Research Symposium. Annapolis, MD, October 2012.

Hubbard, K., Gut, I. and McNutt, P. A novel transcriptomic analysis of embryonic stem cell-derived neurons treated with BoNT/A using RNA-seq. Botulinum Symposium. Dartmouth, MA, August 2012.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

N/A

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

N/A

14) *POST-TENURE POSITION / JOB TITLE*

Biologist IV

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Excelis, Inc., Information Systems Headquarters, 12975 Worldgate Drive, Herndon, VA 20170

16) *POST-TENURE POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the NRC host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the NRC host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| <input checked="" type="checkbox"/> Research/Administrative position with another U.S.- government agency | <input type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign- government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- 1)
- 2)
- 3)
- 4)
- 5)

18) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity

Comments

I learned many new skills and developed bases of knowledge in fields in which I was not previously educated. The McNutt lab was very prolific during my tenure, publishing and presenting frequently. We also explored and implemented many new routes of research which are currently ongoing.

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date

Comments

Without the skills I obtained during my Associateship, I would not have landed this new job.

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

The lab was well funded and equipment was easily accessible. This was overall a very positive experience.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

The mentorship of Dr. McNutt has been outstanding. He gives you every chance to succeed (publish, speak, patent, etc...)

LPR SUPPORT

7 Quality of administrative support from the **L**aboratory (e.g., NIST, NRL, IWR, FHWA) NRC **P**rogram **R**epresentative (LPR)

Comments

I never really dealt with people at this level.

NRC SUPPORT

7 Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

The travel approval process is a little circuitous , but all-in-all dealing with administrative support was relatively smooth.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator
No handwritten signature required;

*but you may upload a scanned
signature file below:*

Linda Sligh: lsligh@nas.edu
Asha Soutar: asoutar@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. December 2014

Proj/Act ID#

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|---|--|
| 1) Associate Last or Family Name | First Name | M.I. |
| Kaini | Ramesh | R |
| 2) FORWARDING Address (to which your tax statement will be mailed) Residence or Institution Street City, State Zip | | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: |
| 3) Today's Date January 28, 2016 | | Dates of Tenure from January 3, 2013 to January 2, 2016 |
| 4) Host Agency AMRMC (e.g., AFRL) | Laboratory or Center USAISR (e.g., Wright Patterson AFB) | Division / Directorate / Department Ocular Trauma (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) Wang Heuy-Ching | | |

6) **TITLE OF RESEARCH PROPOSAL**

Transplantation of stem cells isolated from mouse iPSCs-derived self-formed optic cups in laser-injured retina

7) **SUMMARY OF RESEARCH DURING TENURE** Itemize significant findings in concise form, utilizing key concepts/words.

- 1) **Optimize maintainance and propogation of human PiPS cells in a defined and xenofree condition.**
- 2) **Xenofree differentiation of hiPS cells into neuro-retina**
- 3) **Generation of photoreceptors like cells from human iPS cells**
- 4) **Studied the dynamics of extracellular matrix remodeling during retinogenesis**
- 5) **Formulate a research plan on using stem-cell released molecule as a therapy in blast-injured retina**
(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) **RESEARCH IN PROGRESS** Describe in no more than 100 words.

1. **To investigate SRM of the iPS-retinal EB under XF conditions by analyzing the growth factors, chemokines, matrix proteins and other factors in CdM, and ECM respectively.**
2. **To investigate the neuroprotective and neuro-regenerative effects of SRM of iPS-retinal EB and iPS-RPE under XF conditions in a retinal degeneration model using ex vivo retina explant model.**
3. **To compare the neuroprotective and neuro-regenerative effects of SRM (cell free therapy) and RPC (cell-based therapy) from iPS-cell-derivatives under XF conditions in a rat model of blast-induced retinal injury.**

9) **PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH**

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) **Publications in peer-reviewed journals**

1. **Kaini, R. R., Shen-Gunther, J., Cleland, J. M., Greene, W. A., & Wang, H. C. (2015). Recombinant xeno- free vitronectin supports self-renewal and pluripotency in protein induced pluripotent stem cells. Tissue Engineering, (ja).**
2. **Muñiz, A., Kaini, R.R., Greene, W. A., Choi, J. H., & Wang, H. C. (2014). Deriving Retinal Pigment Epithelium (RPE) from Induced Pluripotent Stem (iPS) Cells by Different Sizes of Embryoid Bodies. Journal of Visualized Experiments: JoVE, (96).**
3. **Wang, H. C., Greene, W. A., Kaini, R. R., Shen-Gunther, J., Chen, H. I. H., Cai, H., & Wang, Y. (2014). Profiling the microRNA Expression in Human iPS and iPS-derived Retinal Pigment Epithelium. Cancer Informatics, 13(Suppl 5), 25.**
4. **Greene, W. A., Muñiz, A., Plamper, M. L., Kaini, R. R., & Wang, H. C. (2014). MicroRNA Expression Profiles of Human iPS Cells, Retinal Pigment Epithelium Derived From iPS, and Fetal Retinal Pigment Epithelium. Journal of Visualized Experiments, (88),**

e51589-e51589.

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

1. Kaini, R.R., Shen-Gunther, J., Greene, W.A., Wang, H.C. Matrix proteins expression in human induced pluripotent stem cells derived retinal organoids. (In preparation)
2. Kaini, R.R., Wang, H.C. Derivation of retinal precursor cells from human protein-induced pluripotent stem cells in a defined and xeno-free condition. (In preparation)
3. Greene, W.A., Burke, T.A., Por E.A., Kaini, R.R., Wang, H.C. Secretion Profile of Induced Pluripotent Stem Cell-Derived Retinal Pigment Epithelium during Wound Healing. (Submitted)

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

1. Kaini, R., Golden, D., Burke, T. A., & Wang, H. C. H. Derivation of retinal progenitors from human induced-pluripotent stem cells in a xeno-free defined condition. ISSCR 12 th Annual Meeting, June 18-21, 2014, Vancouver, BC, Canada

Domestic

1. Kaini, R., Golden, D., Burke, T. A., & Wang, H. C. H. Extracellular matrix remodelling during 3D retinal differentiation of human induced pluripotent stem cells. ARVO Annual Meeting, Feb 16-19, 2015, Denver, CO
2. Kaini, R., Golden, D., Burke, T. A., & Wang, H. C. H. Long term maintainance and propogation of protein induced pluripotent stem cells in a defiend, xeno-free condition. World Stem Cell Summit, Dec 3- 5, 2014, San Antonio, TX
3. Wang H.C., Kaini R.R. Matrix proteins and retina development in a 3D in vitro system. TERMIS 2014, Boston ,MA
4. Wang, Heuy-Ching, Kaini, Ramesh; Burke, Teresa A; Golden, Dallas; Johnson, Anthony J . Matrix proteins and retina development in a 3D in vitro system. World Stem Cell Summit, Dec 3-5, 2014, San Antonio, TX
5. Kaini, R., Johnson, A. J., Burke, T. A., Golden, D., & Wang, H. C. H. Xeno-free 3D retinal differentiation of human induced-pluripotent stem cells. ARVO Annual Meeting, May 4-8, 2014, Orlando, FL

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

Staff Scientist

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Ocular Trauma, USAISR

16) *POST-TENURE POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|---|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | |
| <input type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input checked="" type="checkbox"/> Other (Please specify, possible) ORISE |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- 1)
- 2)
- 3)
- 4)
- 5)

18) APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

5 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

7 How the NRC Research Associateship award affected your career to date
Comments

LAB SUPPORT

5 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

5 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)
Comments

LPR SUPPORT

5 Quality of administrative support from the Laboratory Program Representative (LPR)
Comments

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

10 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

You guys were awesome!

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator

No handwritten signature required;

but you may upload a scanned

signature file below:

Leah Probst: lprobst@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. October 2015

Proj/Act ID#

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NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|--|--|
| 1) Associate Last or Family Name | First Name | M.I. |
| Miller | Christine | L |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | |
| Residence or Institution Street City, State Zip | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: | |
| 3) Today's Date | | |
| Dates of Tenure from Feb 4 2012 to February 3, 2016 | | |
| 4) Host Agency AISR (e.g., AFRL) | Laboratory or Center Dr. Kai P Leung (e.g., Wright Patterson AFB) | Division / Directorate / Department Dental and Trauma Research, ISR (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) Dr. Kai P Leung | | |

6) **TITLE OF RESEARCH PROPOSAL**

Identification of regulatory RNAs of mixed species biofilms associated with chronic war wounds

7) **SUMMARY OF RESEARCH DURING TENURE** Itemize significant findings in concise form, utilizing key concepts/words.

- 1) **Optimized protocol to isolate, identify, and categorize small RNAs (sRNAs) for the discovery of small regulatory RNAs.**
- 2) **Utilized a custom RNA-sequencing method to unbiasedly capture the global transcriptome response of pathogens typically present in war wounds and which hinder healing.**
- 3) **Used an in vitro model to investigate the interactions of *P. aeruginosa* and *S. aureus* in biofilm and planktonic cultures**
- 4) **Discovered sRNAs that play a key role in modulating interspecies interactions in the biofilm, and required for the adaptive switch between acute and chronic infection phenotypes.**
- 5) **Generated numerous protocols to genetically engineer *P. aeruginosa* and analyze phenotypes of various mutants.**

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) **RESEARCH IN PROGRESS** Describe in no more than 100 words.

All my tenure's work has been summarized and submitted to journals and I am awaiting response from the reviewers.

9) **PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH**

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

- a) Publications in peer-reviewed journals
- b) Books, book chapters, other publications
- c) Manuscripts in preparation, manuscripts submitted

Miller, CL, Chen T, Chen P, Leung KP. 2015. Genome sequence of a highly virulent *Pseudomonas aeruginosa* strain, VA-134, isolated from burn patient. Genome Announcements. manuscript accepted.

Miller CL, Van Laar TA, Chen T, You T, Leung KP. 2015. Global transcriptome responses including small RNAs during mixed-species interactions with methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Manuscript submitted.

Miller CL, Romero M, Chen T, Heeb S, Karna SL, Leung KP. 2015. RsmW, *Pseudomonas aeruginosa* small non-coding RsmA-binding RNA upregulated in biofilm versus planktonic growth conditions. Manuscript submitted, responding to reviewers.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

▪ 2nd Annual an Antonio Postdoctoral Research Forum, UTHSC San Antonio 2014

Poster: Identification of novel small RNAs in *Pseudomonas aeruginosa* involved in biofilm formation, antibiotic tolerance, and mixed-species interactions using RNA sequencing

▪ 114th American Society for Microbiology, Boston Massachusetts 2014

Poster: Identification of novel small RNAs in *Pseudomonas aeruginosa* involved in biofilm formation, antibiotic tolerance, and mixed-species interactions using RNA sequencing

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

10 min talk for NRC Supporters- ISR

ISR Seminar - Dec 9 2015- ISR

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

Adjunct Faculty for Microbiology- St Philips College

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Address: 1801 Martin Luther King Dr, San Antonio, TX 78203

Phone: (210) 486-2000

16) *POST-TENURE POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | |
| <input type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input checked="" type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

1)

2)

3)


4)

5)

18) APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

 Development of knowledge, skills, and research productivity

Comments

LONG TERM VALUE

 How the NRC Research Associateship award affected your career to date

Comments

LAB SUPPORT

 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.


Comments

ADVISER/MENTOR SUPPORT

 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)


Comments

LPR SUPPORT

 Quality of administrative support from the Laboratory Program Representative (LPR)

Comments

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator
No handwritten signature required;

*but you may upload a scanned
signature file below:*

Christine Lindsay Miller

Leah Probst: lprobst@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. October 2015

Proj/Act ID#

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NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|---|--|
| 1) Associate Last or Family Name | First Name | M.I. |
| O'Hearn | Aileen | E |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | |
| Residence or Institution Street City, State Zip | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: | |
| 3) Today's Date | | |
| Dates of Tenure from April 1, 2013 to April 1, 2016 | | |
| 4) Host Agency AMRMC (e.g., AFRL) | Laboratory or Center USAMRIID (e.g., Wright Patterson AFB) | Division / Directorate / Department Diagnostic Systems Division (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) Dr. Randall Schoepp | | |

6) TITLE OF RESEARCH PROPOSAL

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Development of a pan-Flavivirus and pan-Alphavirus IgG test to be incorporated in a panel of African viral diagnostics
 - 2) Development of a multi-target serosurveillance test for identifying viral pathogens in West Africa
 - 3) Serosurvey of a Sierra Leonean population for the presence of viral pathogens, and identification of public health threats
 - 4) Development and testing of a Lassa virus diagnostic testing panel for identifying human Lassa Fever cases
 - 5) On-site support during the West African Ebola outbreak
- (USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Preparing manuscripts for submission

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

b) Books, book chapters, other publications

Schoepp RJ and O'Hearn AE (in press) (2016). "Arenaviruses", in Molecular detection of animal viral pathogens. CRC Press.

c) Manuscripts in preparation, manuscripts submitted

O'Hearn AE, Voorhees MA, Koehler JW, Olschner SP, Wauquier N, and Schoepp RJ (in prep): Serological and viral kinetics of Lassa virus infection in humans.

O'Hearn AE, Voorhees MA, Fetterer DP, Clements T, Wauquier N, Schoepp RJ (in prep): Seroprevalence of viral pathogens in Sierra Leone.

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

American Society of Tropical Medicine and Hygiene 63rd annual meeting, New Orleans, poster presentation: Development of advanced seroassays to broaden diagnostic and surveillance capability in West Africa.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

National Cancer Institute (NCI): Combating disease in the developing world: Diagnostics and surveillance in West Africa.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

Science Education Fellow

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Howard Hughes Medical Institute

16) *POST-TENURE POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|---|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | |
| <input type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input checked="" type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- 1)
- 2)
- 3)
- 4)
- 5)

18) *APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

4 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

9 How the NRC Research Associateship award affected your career to date
Comments

LAB SUPPORT

7 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

8 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)

Comments

LPR SUPPORT

4 Quality of administrative support from the Laboratory Program Representative (LPR)

Comments

Did not interact with them much.

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

8 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

Usually very helpful with any aspect of tenure.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Very much liked the NRC associateship program. I was happy with the benefits, and if the program develops further, maybe think about adding options for retirement savings. It is a heavy concern while doing a post-doc, being in your 30s, starting a family, and not having the ability to start a retirement plan.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator

*No handwritten signature required;
but you may upload a scanned
signature file below:*

Aileen E O'Hearn

Leah Probst: lprobst@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. October 2015

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NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|---|---|
| 1) Associate Last or Family Name | First Name | M.I. |
| Rose | Lloyd | F |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | |
| Residence or Institution Street City, State Zip | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: | |
| 3) Today's Date | | |
| Dates of Tenure from November 4, 2012 to October 2, 2015 | | |
| 4) Host Agency AMRMC (e.g., AFRL) | Laboratory or Center USAISR (e.g., Wright Patterson AFB) | Division / Directorate / Department DTRD (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) | | |
| Kai P. Leung | | |

6) *TITLE OF RESEARCH PROPOSAL*

Assessment of Wound Bed Modulation Prior to Skin Grafting in a Porcine Model

7) *SUMMARY OF RESEARCH DURING TENURE* Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Establishment of a porcine model of skin loss correlating thickness of autologous skin graft with amount of contraction after 120 days.
- 2) Autologous skin grafts grafted onto fat (as opposed to grafting onto deeper tissues) resist contractile forces induced by myofibroblasts.
- 3) Burn wounds have increased inflammatory markers and have increased levels of wound contraction compared to skin loss by non-burn mechanisms.
- 4) Application of ultra-high dose gentamicin to the wound bed induces an anti-angiogenic gene expression profile in vivo as well as inducing genetic and phenotypic alterations in endothelial cells and macrophages in tissue culture.
- 5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) *RESEARCH IN PROGRESS* Describe in no more than 100 words.

Primary research project focuses on the use of pharmacologic agents to modulate the status of the wound bed prior to or during grafting. These agents are anti-inflammatories, antibiotics, other antimicrobials or other factors that might influence graft take, wound healing or final scar outcome. The hypothesis is that alteration of the wound microenvironment can alter the healing trajectory, resulting in reduced contraction or hypertrophic scar.

9) *PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

Chan RK, Rose LF, Wu JC, Tucker DI, Chan MM, Christy R, Hale RG, Leung KP. Autologous Graft Thickness Affects Scar Contraction and Skin Quality in a Porcine Excisional Wound Model. Plastic and Reconstructive Surgery - Global Open. 2015 Aug 10;3(7):e468. doi: 10.1097/GOX.0000000000000426. eCollection 2015 Jul.

Rose LF, Wu JC, Carlsson AH, Tucker DI, Leung KP, Chan RK. Recipient wound bed characteristics affect scarring and skin graft contraction. Wound Repair and Regeneration. 2015 Feb 13. doi: 10.1111/wrr.12267.

Rowan MP, Cancio LC, Elster EA, Burmeister DM, Rose LF, Natesan S, Chan RK, Christy RJ, Chung KK. Burn wound healing and treatment: review and advancements. Critical Care. 2015 Jun 12;19:243. doi: 10.1186/s13054-015-0961-2.

Wu JC, Rose LF, Christy RJ, Leung KP, Chan RK. Full-Thickness Thermal Injury Delays Wound Closure in a Murine Model. *Advances in Wound Care*. 2015 Feb 1;4(2):83-91.

Rose LF and Chan RK. The Burn Wound Microenvironment. *Advances in Wound Care*. 2014 Jun 25; doi:10.1089/wound.2014.0536.

Li Z, Roussakis E, Koolen PGL, Ibrahim AM, Kim K, Rose LF, Wu J, Nichols AJ, Baek YJ, Birngruber R, Apiou G, Matyal R, Huang T, Chan R, Lin S, Evans CL. Non-invasive Transdermal Two-dimensional Mapping of Skin, Burn, and Graft Oxygenation with a Rapid-Drying Liquid Bandage. *Biomedical Optics Express*. 2014 Oct 1;5(11):3748-64.

b) Books, book chapters, other publications

N/A

c) Manuscripts in preparation, manuscripts submitted

Rose LF, Carlsson AH, Tucker DI, Wu JC, Leung KP, Chan RK. Effect on Scar Contraction and Skin Quality of Tangential Excision and Grafting of Full-Thickness Burn Wounds in a Porcine Contact-Burn Wound Model. Manuscript in preparation.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

N/A

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

N/A

Domestic

Lloyd F. Rose, Melissa Olekson, Kai P. Leung, Rodney K. Chan. High Dose Gentamicin Modulates Angiogenesis-Related Genes and Phenotypes Both In Vitro and in Vivo. Poster presentation @ San Antonio Postdoctoral Research Forum, San Antonio, TX. September 2015.

Lloyd F. Rose, Melissa Oleksson, Kai P. Leung, Rodney K. Chan. High Dose Gentamicin Modulates Angiogenesis-Related Gene Expression Both In Vitro and In Vivo. Oral presentation @ the Military Health System Research Symposium, Ft Lauderdale, FL. August 2015

Lloyd F. Rose. The Pathogenesis of Wound Healing. Invited Speaker @ the Association of Primate Veterinarians Annual Meeting, San Antonio, TX. October 2014.

Lloyd F. Rose and Rodney K. Chan. The Role of Hypodermis in Contraction and Scarring. Oral presentation @ the Southern Region Burn Conference, Houston, TX. November 2014.

Lloyd F. Rose, Jesse Wu, David I. Tucker, Rodney K. Chan. Characterization of the role of hypodermis in contraction. Poster presentation @ the Mikiten Research Forum, San Antonio, TX. September 2014.

Lloyd F. Rose, Jesse Wu, David I. Tucker, Rodney K. Chan. Characterization of the role of hypodermis in contraction. Poster presentation @ the Military Health Systems Research Symposium, Ft. Lauderdale, TX. August 2014.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

Induction of Cytoskeletal Rearrangements Vaccinia Virus Host Range Gene K1L. Department of Biology Research Seminar. Trinity University. April 2015.

Analysis and Optimization of Skin Quality after Replacement Therapy. ISR Research Seminar. US Army Institute of Surgical Research. April 2014.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

N/A

14) *POST-TENURE POSITION / JOB TITLE*

Assistant Portfolio Manager

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

**U.S. Army Medical Research and Materiel Command
Clinical & Rehabilitative Medicine Research Program
810 Schreider Street, BLDG 722
Fort Detrick, MD 21702-5012**

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input checked="" type="checkbox"/> Contract or temporary position at the host Agency Abbreviate Host Laboratory/Center <u>AMRMC</u> | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| <input type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* **Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.**

- 1)
- 2)
- 3)
- 4)
- 5)

18) *APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

8 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

10 How the NRC Research Associateship award affected your career to date
Comments

There was a lot of opportunity to network and find connections that could lead to future employment, as happened in my circumstance. The position I am moving to was the direct result of attendance at the Military Health Systems Research Symposium in August 2015.

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments
Could not have been better.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)
Comments
Many sources of mentoring were available, each with their own strengths and insight.

LPR SUPPORT

10 Quality of administrative support from the Laboratory Program Representative (LPR)
Comments

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

8 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)
Comments

I never had any significant problems with any of the administrative support. This is especially notable after seeing fellow postdocs with other funding organizations go through all sorts of administrative issues.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator

*No handwritten signature required;
but you may upload a scanned
signature file below:*

Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. July 2015

Proj/Act ID#

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

NRC Research Associateship Programs

FINAL REPORT

| | | |
|--|--|--|
| 1) Associate Last or Family Name | First Name | M.I. |
| Salas | Margaux | M |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | |
| Residence or Institution Street City, State Zip | FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail: margaux.m.salas.vol@mail.mil | |
| 3) Today's Date | | |
| October 30, 2015 | | |
| Dates of Tenure | | |
| from October 10, 2012 to October 1, 2015 | | |
| 4) Host Agency (e.g., AFRL) | Laboratory or Center (e.g., Wright Patterson AFB) | Division / Directorate / Department Pain Management Task Area (e.g., High-Speed Propulsion) |
| 5) Name of Laboratory Adviser (and USMA Mentor, if applicable) | | |
| John Clifford, PhD | | |

6) *TITLE OF RESEARCH PROPOSAL*

The role of curcumin in thermal injury-evoked hyperalgesia

7) *SUMMARY OF RESEARCH DURING TENURE* Itemize significant findings in concise form, utilizing key concepts/words.

- 1) **Tetrodotoxin Attenuates Thermal Hyperalgesia in a Rat Full Thickness Thermal Injury Pain Model**
- 2) **Curcumin is an Effective Analgesic for Burn Pain: Evidence from Animal and Human Tissue Based Experiments**
- 3) **Resiniferatoxin: A Potential Burn Analgesic for Point of Injury/Battlefield**
- 4)
- 5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) *RESEARCH IN PROGRESS* Describe in no more than 100 words.

*** Hemodynamic responses to analgesic for pain management in combat patients transported from POI to first MTF in Israel Defense Forces and U.S. Military**

***Prospective, Randomized, Double-Blind Controlled Pilot Study to compare Topical Voriconazole to Placebo as a Pain Reducing Agent at Skin Donor Sites**

9) *PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

1. **Clifford JL, Fowler M, Hansen JJ, Cheppudira B, Nyland JE, Salas MM, McGhee LL, Petz LN, and Loyd DR. State of the Science Review: Advances in pain management in wounded service members over a decade of war. Journal of Trauma Acute Care Surgery, 77(3 Suppl 2) S228-236, 2014.**
2. **M.M Salas, M.K. McIntyre, D. Wong, W. Korz, J. L. Clifford. 2015. Tetrodotoxin attenuates thermal hyperalgesia and mechanical allodynia in a rat model of full thickness thermal injury. Neuroscience Letters, Accepted October 2015.**

b) Books, book chapters, other publications

1. **M.M. Salas, B.P. Cheppudira, M. Fowler, L. Petz, DI Devore, and J.L. Clifford. Analgesic and anti-inflammatory properties of curcumin: application for burn wounds. In Curcumin: Synthesis, Emerging Role in Pain management and Health Implications, Daniel Pouliquen (Ed.), Nova Science Publishers, 2014.**

c) Manuscripts in preparation, manuscripts submitted

1. M.M. Salas, J. Hayden, T. Slater, M. Fowler, J. L. Clifford , L. N. Petz, M. J. Iadarola, D.R. Loyd. Resiniferatoxin attenuates pain behaviors in a rat model of full thickness thermal injury. In preparation.

2. M.M. Salas, A. Greer, L.N. Petz, and J.L. Clifford. Curcumin attenuates thermal hyperalgesia in a rat full thickness thermal injury model by influencing inflammation signaling. In preparation.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

N/A

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

NONE

Domestic

1. Arizpe H.M., Greer A., Salas M.M, Fowler M., Maj Petz L.N., LTC Novak J., Averitt D.L., Clifford J.L. Immunohistochemical analysis of the inflammatory response in a rat model of full thickness thermal injury. Military Health System Research Symposium (MHSRS), 2013.

2. Salas M.M., Jones J., Fowler M., Averitt D.L., Maj Petz L.N., Col Renz E.M., Maj Maani M.D., Garza T.H., Sueltenfuss R.N., Orman J., Clifford J.L. Pain medication profile for severely burned military service members in OIF and OEF. Military Health System Research Symposium (MHSRS), 2013.

3. Salas M.M., Jones J., Fowler M., Averitt D.L., Maj Petz L.N., Col Renz E.M., Maj Maani M.D., Garza T.H., Sueltenfuss R.N., Orman J., Clifford J.L. Pain medication profile for severely burned military service members in Operations Iraqi Freedom and Enduring Freedom. Society for Neuroscience Annual Meeting, 2013.

4. Gibbons R.V., Salas M.M., Jones J., Fowler M., Petz L.N., Hansen J., Bakewell T., Orman J.A., Clifford J.L. USAISR Burn Clinic Pain medication Usage Patterns for severely burned military service members. Military Health System Research Symposium (MHSRS), 2014.

5. Salas M.M., Greer A., Fowler M., Petz L.N., and Clifford J.L. Curcumin Attenuates Thermal Hyperalgesia in a Rat Full Thickness Thermal Injury Model by Influencing Inflammation Signaling. Military Health System Research Symposium (MHSRS), 2014.

6. Salas M.M., Greer A., Fowler M., Petz .LN., and Clifford J.L. Curcumin Attenuates Thermal Hyperalgesia in a Rat Full Thickness Thermal Injury Model by Influencing Inflammation Signaling. Society for Neuroscience Annual Meeting, 2014.

7. Salas M.M., Petz L., McIntyre M.K., Korz W., Wong D., Clifford J.L. Tetrodotoxin Attenuates Thermal Hyperalgesia in a Rat Full Thickness Thermal Injury Model. Military Health System Research Symposium (MHSRS), 2015.

8. Salas M.M., Trevino A., Greer A., Clifford J.L. Curcumin is an Effective Analgesic for Burn Pain: Evidence from Animal and Human Tissue-based Experiments. Military Health System Research Symposium (MHSRS), 2015.

9. Benov A., Salas M.M., Helit N., Antebi B., Shina A., Chung K., Cap A.P., Darlington D.N., Galssberg E., Yitzhak A. Pain Management at Point of Injury in IDF: Retrospective Analysis 1997-2014. Military Health System Research Symposium (MHSRS), 2015.

10. Salas M.M., Bebart V., Barnard E., Petz L., Tyner S., Gibbons R., Benov A. Battlefield Analgesics: A Retrospective Comparison between the US Army and Israel Defense Forces. Military Health System Research Symposium (MHSRS), 2015.

11. Salas M.M., Petz L., McIntyre M.K., Korz W., Wong D., Clifford J.L. Tetrodotoxin Attenuates Thermal Hyperalgesia in a Rat Full Thickness Thermal Injury Model. American Pain Society Meeting, 2015

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

1. Basic Science Pain Research at the US Army Institute of Surgical Research (RTX). American Pain Society 2013, New Orleans

2. **Resiniferatoxin Attenuates Pain Behaviors in a Rat Model of Full Thickness Thermal Injury.** MHSRS 2013, Ft. Lauderdale Florida
3. **From Inflammation and Interactions to Blisters, Burns, and Analgesics.** USAISR Seminar Series, 2013
4. **Analgesic and Wound Healing Responses to Peripheral Analgesic Treatments in a Full Thickness Burn Model.** National Research Council Site Visit, USAISR 2013
5. **Tetrodotoxin: How a Neurotoxin Can Work for You.** National Research Council Site Visit, USAISR 2014
6. **The Institute of Surgical Research: Pain Management Task Area.** CEO Day, USAISR 2014
7. **Battlefield Pain Management Task Area USAISR.** USAISR 2014
8. **Curcumin: A Prototype Anti-inflammatory Therapeutic for Burn Pain and Wound Healing.** Burn and Trauma Research Workgroup. BAMMC Burn Center 2014
9. **Studies on a Novel Toxin-Based Analgesic: Tetrodotoxin.** Burn and Trauma Research Workgroup. BAMMC Burn Center 2014
10. **Battlefield Pain Management: Fulfilling the Unique Needs of the Department of Defense.** Texas State University-San Marcos Seminar Series 2015
11. **The Science of Pain Management.** BAMMC Clinical Health Psychology Work Group 2015
12. **Battlefield Analgesics: A Retrospective Comparison Between the US Army and Israel Defense Forces.** MHSRS 2015

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

2015

Hemodynamic Responses to Analgesics for Pain Management in Combat Patients Transported from Point of Injury to First Medical Treatment Facility in Israel Defense Forces and U.S. Military
\$462K/2 years- Associate Investigator
Defense Health Program/JPC6/Combat Casualty Care Research Program FY15 DHP 6.7 #DM150035

2015

Prospective, Randomized, Double-Blind Controlled Pilot Study to Compare Topical Voriconazole to Placebo as A Pain Reducing Agent at Skin Donor Sites.
\$354K/2 years- Associate Investigator
FY15 DHP D6.7 #D6.7_15_C2_I_15_J9_1287

14) *POST-TENURE POSITION / JOB TITLE*

Clinical Research Scientist- Pain Clinic- BAMC

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Clinical Research Scientist
Integrative Pain Management Clinic
Brooke Army Medical Center
3551 Roger Brooke Drive
JB SA Fort Sam Houston, TX 78234

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input checked="" type="checkbox"/> Contract or temporary position at the host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | <input type="checkbox"/> Research/administration position with a non profit |
| <input checked="" type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) *SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE* **Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.**

- 1)
- 2)
- 3)
- 4)
- 5)

18) *APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

8 Development of knowledge, skills, and research productivity

Comments

Good for staying within the military sector, not sufficient if going back into academia.

LONG TERM VALUE

8 How the NRC Research Associateship award affected your career to date

Comments

Gave me the opportunity to understand the nature of military research and gave me the opportunity to begin a career within the military research sector.

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

Excellent facilities in the USAISR.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory Adviser (USMA Mentor, if applicable)

Comments

John Clifford was excelent in mentoring my growth and development as a Post-doc in terms of publications, presentations, and grant writing. He gave me the flexibility and freedom to express my scientific opinion and style.

LPR SUPPORT

10 Quality of administrative support from the Laboratory Program Representative (LPR)

Comments

Dr. Dubick was an excellent and supportive mentor for me. He gave both guidance in NRC matters and in career paths and opportunities.

NRC RESEARCH ASSOCIATESHIP PROGRAMS SUPPORT

9 Quality of administrative support. Please assess the support you received from the Fellowships Office (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

Administrative support was great. The only problem I ever had was receiving reimbursement for travel in a timely manner. Otherwise, NRC administrative support was easy to contact and quick to answer. Thank you for all your support.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your Program Coordinator

*No handwritten signature required;
but you may upload a scanned
signature file below:*

Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id#

Rev. July 2015

Proj/Act ID#

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine
National Research Council

Research Associateship Programs

FINAL REPORT

| | | | |
|--|------------------------------|---|------|
| 1) Associate Last or Family Name | | First Name | M.I. |
| Van Laar | | Tricia | A |
| 2) FORWARDING Address (to which your tax statement will be mailed) | | FORWARDING Phone(s) and E-Mail (if known) Home Phone: | |
| Residence or Institution | | Alt. Phone: | |
| Street City, State Zip | | Preferred E-mail: | |
| 3) Today's Date | | Dates of Tenure | |
| July 13, 2015 | | from April 9, 2012 to July 29, 2015 | |
| 4) Host Agency | Laboratory or Center | Division / Directorate / Department | |
| AMRMC | JBSA Ft Sam Houston | ISR/DTRD | |
| (e.g., AFRL) | (e.g., Wright Patterson AFB) | (e.g., High-Speed Propulsion) | |
| 5) Name of Laboratory NRC Adviser (and USMA Mentor, if applicable) | | | |
| Dr. Kai Leung | | | |

6) TITLE OF RESEARCH PROPOSAL

Transcriptome Analysis of War Wound Pathogens

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Contributed to gene sequencing of multi-drug resistant *Klebsiella pneumoniae*
- 2) Performed transcriptome analysis of multi-drug resistant *K. pneumoniae* and identified numerous genes for downstream analysis in combating multi-drug resistant *K. pneumoniae*. Also described molecular mechanisms for significant morphological changes.
- 3) Performed transcriptome analysis of mixed species biofilm and planktonic cultures of *Staphylococcus aureus* and *Pseudomonas aeruginosa* and identified numerous ORFs necessary for competition between these two species.
- 4) Performed transcriptome analysis of persister cells of *P. aeruginosa* to identify ORFs necessary for persister cell formation, and therefore lack of healing in *P. aeruginosa* infected wounds.
- 5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Continued analysis of ORFs important for persister cell formation in *Pseudomonas aeruginosa* to identify targets for potential drug therapy to combat infections highly resistant to drug therapy.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

Childers BM, Van Laar TA, You T, Clegg S, Leung KP. 2013. MrkD1P from *Klebsiella pneumoniae* strain IA565 allows for coexistence with *Pseudomonas aeruginosa* and protection from protease-mediated biofilm detachment. *Infect Immun* 81:4112–4120

Van Laar TA, Chen T, Childers BM, Chen P, Abercrombie JJ, Leung KP. 2014. Genome sequence of a multidrug-resistant strain of *Klebsiella pneumoniae*, BAMC 07-18, isolated from a combat injury wound. *Genome Announc* 2(6):e01230-14.

Van Laar TA, Chen T, You T, Leung KP. 2015. Sublethal concentrations of carbapenems alter cell morphology and genomic expression of *Klebsiella pneumoniae* biofilms. *Antimicrob Agents Chemother* 59:1707–1717

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

Van Laar TA*, Miller CL*, Chen T, You T, Leung KP. 2015. Transcriptome analysis of *Pseudomonas aeruginosa* and *Staphylococcus aureus* mixed species planktonic and biofilm cultures (in preparation)

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

Interscience Conference on Antimicrobial Agents and Chemotherapies, Denver, CO Sep 2013

The Effect of Imipenem on Biofilms of a Multi-Drug Resistant Clinical Isolate of *Klebsiella pneumoniae*

General Meeting of the American Society for Microbiology, Boston, MA May 2014

Transcriptome Analysis of Persister Cells of *Pseudomonas aeruginosa*

T. A. Van Laar, T. Chen, and K. P. Leung

Pseudomonas aeruginosa is a Gram-negative bacterium found ubiquitously in the environment. *P. aeruginosa* is also an important opportunistic human pathogen capable of causing extreme respiratory diseases and wound infections, leading to severe morbidity and mortality. Many *P. aeruginosa* infections are resistant to antibiotic therapy. This can be due to a number of factors, including inherent antibiotic resistance and the formation of biofilms in which the presence of persister cells contributes partly to the drug-resistant phenotype of biofilms. Persister cells are a subpopulation of cells which are genetically identical to the rest of the biofilm cell population, but experience a transiently antibiotic resistant phenotype. The mechanisms behind persister cell formation are poorly understood. Therefore we have performed RNA sequencing of persister cells of *P. aeruginosa* strain PAO1 in order to determine the genomic regulatory mechanism(s) responsible for transforming cells to the persister phenotype. We found that 238 open reading frames (ORFs) were upregulated while 428 ORFs were downregulated in the persister cell fraction when compared to stationary phase cells. Categories upregulated include genes involved in DNA repair, antibiotic resistance, peptidoglycan biosynthesis and pyocin production, while genes responsible for motility, metabolism, and biofilm formation were downregulated in persister cells. Quantitative real-time PCR (qRT-PCR) analysis confirmed selected hits. We are currently screening a PAO1 transposon mutant library in order to identify the ORFs that are essential for the development of the persister cell phenotype. We found a number of knockouts that could lead to differential persister cell formation. Understanding the mechanisms behind persister cell formation will allow for the more successful treatment of *P. aeruginosa* infections.

Military Health System Research Symposium, Fort Lauderdale, FL August 2014

Sublethal Concentrations of Carbapenems Change Cell Morphology and Genomic Expression in *Klebsiella pneumoniae*

T.A. Van Laar, T. Chen, T. You, and K.P. Leung

Background: *K. pneumoniae* is an important nosocomial pathogen of surgical sites and combat wounds with many strains displaying multi-drug resistance. *K. pneumoniae* uses biofilm formation as a major virulence factor, contributing to increased antibiotic resistance and impaired clearance. A strain of *K. pneumoniae* isolated from a wound demonstrated resistance to commonly used antibiotics, but sensitivity to the broad-spectrum β -lactam class carbapenems. We were interested in determining how sublethal concentrations of carbapenems affect overall fitness of *K. pneumoniae* biofilms.

Methods: *K. pneumoniae* biofilms were treated for 2 or 24 hours with sublethal concentrations of carbapenems. Scanning electron microscopy (SEM) of untreated and treated biofilms was used to observe phenotypic changes while RNA sequencing (RNAseq) was used to determine global gene expression and regulation of untreated and treated biofilms.

Results: SEM showed striking phenotypic changes in treated biofilms, including rounding, blebbing, and dimpling of treated cells. These changes are transient and dependent on continued antibiotic presence. Comparative transcriptome analysis using RNAseq technology identified a large number of ORFs differentially regulated in response to imipenem treatment. Some of the changes in gene expression are indicative of bacterial stress response, while other changes include motility, transport, and metabolism. qRT-PCR has validated the general trend of some of these differentially regulated ORFs.

Conclusions: Treating *K. pneumoniae* biofilms with sublethal concentrations of carbapenems induced wide-range phenotypic and gene expression changes. The understanding of how sublethal amounts of carbapenems alter fitness and pathogenic potential of *K. pneumoniae* biofilm cells highlights the importance of therapy compliance and investigation of possible drug combinations for infection eradication.

UT Health Science Center San Antonio Postdoctoral Research Symposium, San Antonio, TX September 2014

Sublethal Concentrations of Carbapenems Change Cell Morphology and Genomic Expression in Klebsiella Pneumoniae

T.A. Van Laar, T. Chen, T. You, and K.P. Leung

Background: *K. pneumoniae* is an important nosocomial pathogen of surgical sites and combat wounds with many strains displaying multi-drug resistance. *K. pneumoniae* uses biofilm formation as a major virulence factor, contributing to increased antibiotic resistance and impaired clearance. A strain of *K. pneumoniae* isolated from a wound demonstrated resistance to commonly used antibiotics, but sensitivity to the broad-spectrum β -lactam class carbapenems. We were interested in determining how sublethal concentrations of carbapenems affect overall fitness of *K. pneumoniae* biofilms.

Methods: *K. pneumoniae* biofilms were treated for 2 or 24 hours with sublethal concentrations of carbapenems. Scanning electron microscopy (SEM) of untreated and treated biofilms was used to observe phenotypic changes while RNA sequencing (RNAseq) was used to determine global gene expression and regulation of untreated and treated biofilms.

Results: SEM showed striking phenotypic changes in treated biofilms, including rounding, blebbing, and dimpling of treated cells. These changes are transient and dependent on continued antibiotic presence. Comparative transcriptome analysis using RNAseq technology identified a large number of ORFs differentially regulated in response to imipenem treatment. Some of the changes in gene expression are indicative of bacterial stress response, while other changes include motility, transport, and metabolism. qRT-PCR has validated the general trend of some of these differentially regulated ORFs.

Conclusions: Treating *K. pneumoniae* biofilms with sublethal concentrations of carbapenems induced wide-range phenotypic and gene expression changes. The understanding of how sublethal amounts of carbapenems alter fitness and pathogenic potential of *K. pneumoniae* biofilm cells highlights the importance of therapy compliance and investigation of possible drug combinations for infection eradication.

12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars.

13) PROFESSIONAL AWARDS RECEIVED DURING TENURE

14) POST-TENURE POSITION / JOB TITLE

Assistant Professor of Microbiology

15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION

California State University, Fresno
Department of Biology
2555 East San Ramon Ave MS/73
Fresno, CA 93740

16) POST-TENURE POSITION STATUS / CATEGORY Please indicate only one.

- | | |
|--|---|
| <input type="checkbox"/> Permanent position at the NRC host agency | <input type="checkbox"/> Research/administration position in private industry in the U.S. |
| <input type="checkbox"/> Contract or temporary position at the NRC host Agency | <input type="checkbox"/> Research/administration position in private industry outside of the U.S. |
| Abbreviate Host Laboratory/Center _____ | |
| <input type="checkbox"/> Research/Administrative position with another U.S.-government agency | <input type="checkbox"/> Research/administration position with a non profit |
| <input type="checkbox"/> Research/Administrative position with a foreign-government agency | <input type="checkbox"/> Self-employed/consulting |
| <input checked="" type="checkbox"/> Research/teaching position at a U.S. college or university | <input type="checkbox"/> Postdoctoral research |
| <input type="checkbox"/> Research/teaching position at a foreign college or university | <input type="checkbox"/> Other (Please specify, possible) _____ |
| | <input type="checkbox"/> No information provided |

17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- 1)
- 2)
- 3)
- 4)
- 5)

18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity

Comments

I was able to be first author (or co-first author) on 3 manuscripts as well as a co-author on an additional manuscript. This exceeded my expectations of a 3.33 year post-doctoral position.

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date

Comments

I believe that my success at finding a tenure track position can be partially attributed to the successes I have had as an NRC fellow.

LAB SUPPORT

8 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

In-processing was slightly difficult and all of the regulations are confusing (particularly for those responsible for enforcing them), but I imagine this is par for the course at a military installation.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

Dr. Leung gave me a great project to start with and allowed me to explore further interests that aligned with our core goals. He wrote kind letters of recommendation for me and has been supportive of my transition. He has provided timely feedback and given great advice for driving my projects forward.

LPR SUPPORT

10 Quality of administrative support from the Laboratory (e.g., NIST, NRL, IWR, FHWA) NRC Program Representative (LPR)

Comments

NRC SUPPORT

8 Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

The only issue I have ever had with NRC is dealing with travel. Concur is not a user-friendly system and I can spend hours trying to input everything only to have my information kicked back without notice or payment.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator
No handwritten signature required;

**but you may upload a scanned
signature file below:**

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